UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,192	07/02/2003	**Ranajit Pal**	502615.20014	4134

26418 7590 03/31/2009

REED SMITH, LLP
ATTN: PATENT RECORDS DEPARTMENT
599 LEXINGTON AVENUE, 29TH FLOOR
NEW YORK, NY 10022-7650

EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
03/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,192	PAL ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *8-14 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,15 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 4, 2009, has been entered.

2. Claims 1-21 are pending. Claims 8-14 and 16-20 have been withdrawn from consideration as nonelected inventions. Claims 1 and 15 have been amended. Claims 1-7, 15 and 21 are considered in this Office action.

Claim Rejections - 35 USC § 112, first paragraph-Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. (**Prior rejection- maintained**) The rejection of Claims 1-7, 15 and 21 under 35 U.S.C. §112, first paragraph, as failing to comply with the **written description** requirement **is maintained**, for the reasons set forth in the Office actions dated November 20, 2006, May 15, 2007, January 23, 2008, and August 12, 2008, and the reasons set forth below.

In response to Applicant's arguments:

5. Applicant again provides same argument that the claims comply with the **written** description requirement because the phrases "the conformation of any fragment of CD4" and "cryptic epitopes" are conventional in the art. Applicant again asserts that in **the phrase** "the conformation of any fragment of CD4", the only words the Examiner can possibly be asserting to be unconventional are "conformation" and "a fragment of CD4". Then Applicant again goes on to define "conformation of a protein" and "cryptotope" using same citations from Wikipedia (see Appendix B). Applicant further asserts that "Examiner completely fails to address the above arguments as to why the two phrases "the conformation of any fragment of CD4" and "cryptic epitopes" are not conventional in the art are in fact conventional in the art (Emphasis added by Applicant).

6. This argument has been found to be irrelevant in the Final Office action dated August 12, 2008, because Applicant has mischaracterized the Examiner's basis of rejection. The previous Office actions clearly indicated that it was **the structural feature** of "the conformation of any fragment of CD4" that was in question, not **the phrases** of "conformation" and "a fragment of CD4", as Applicant asserted. Claim 1 specifically requires: "...an equivalent of a fragment of CD4 is any molecule that mimics the conformation of any fragment of CD4..." As indicated in the previous Office action (dated August 12, 2008, see Para 6), a fragment of CD4 could be any piece of the CD4 molecule from as small as a two amino acid residue, to as big as the whole CD4 molecule. Such CD4 fragments obviously have totally different conformations. The generic terms "conformation of a protein", "a fragment of CD4" and "cryptotope" (Appendix B) are not descriptive for the specific structure(s) of "the conformation of any fragment of CD4" in the claims.

7. Furthermore, Applicant's argument that "the conformation of any fragment of CD4" and "cryptic epitopes" is conventional in the art is contrary to the specification. The following citation from specification Para [0014]:

"We **have discovered** that a gp120-CD4 covalently bonded complex presents **a specific subset of cryptic epitopes** on gp120 and/or CD4 not present on the uncomplexed molecules. This complex elicits neutralizing antibodies with **novel specificities** and is thus useful in vaccines and immunotherapy against HIV infection" (Emphasis added by the examiner)

In view of specification Para [0014], "**a specific subset of cryptic epitopes"** does not appears to be conventional in the art or known to one of ordinary skill in the art. If "a specific subset of cryptic epitopes" were conventional known in the art as Applicant asserted, there would be no need to "discover" it. However, it is noted that the specification has not provided any description about the structure features of "**a specific subset of cryptic epitopes"**, nor what specific "**novel specificities**" the claimed complex has.

8. Since the specification has not adequately described what specific conformation(s) the alleged "equivalent of a fragment of CD4" mimics, so that it "reveals cryptic epitopes", one of ordinary skill in the art cannot envision what is "any molecule that mimics the confirmation of any fragment of CD4" and reveals "cryptic epitopes". Applicant's argument based on mischaracterizing the Examiner's basis of the rejection is not relevant, therefore, not persuasive. The rejection is maintained.

Claim Rejections - 35 USC § 112, first paragraph-scope of enablement

9. (**Prior rejection- maintained**) The rejection of Claims 1-7, 15 and 21 under 35

U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope with these claims, **is maintained** for the reason of record.

In response to Applicant's arguments:

10. Applicant argues that since the original claims are a part of the disclosure. As such, by definition, the disclosure of the Application must be commensurate in scope with the original claims.

11. This argument is not convincing. Just because the original claims are part of the disclosure does not mean that they provide adequate written description and enabling for the claimed subject matter. Since the instant specification has failed to provide adequate structure description of "the conformation of any fragment of CD4", one of ordinary skill in the art cannot envision what "any molecule" is "that mimics the confirmation of any fragment of CD4" and reveals "cryptic epitopes". As a result, the skilled artisan cannot make the claimed immunogenic complex commensurate in scope with these claims. Rejection is maintained.

12. (**Prior rejection-maintained-extended-restated**) The rejection of Claim 15 under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement **is maintained** and **extended** to Claim 21 for the same reasons as set forth in the Office actions dated November 20, 2006, May 15, 2007, January 23, 2008, and August 12, 2008, and the restated reasons set forth below:

In response to Applicant's arguments:

13. Applicant argues that Claim 15 has been currently amended to be directed to a composition for use in immunotherapy. Such a composition is supported by the Specification, which states that complexes including gp120 bonded to a fragment of CD4 are useful in immunotherapy. Therefore, the rejection should be withdrawn.

14. Applicant's argument is considered. However, the amendment is not sufficient to overcome the rejection. By definition, "immunotherapy" means: "the prevention or treatment of disease with substances that stimulate the immune response". (Compact Oxford English Dictionary, see the attachment to the Office action). The description of the invention in the present application indicates that the claimed gp120-CD4 covalently bonded complex is intended for HIV vaccine and immunotherapy against HIV infection (see Para [0014]). In support of the claims, the specification has shown that the gp120-DID2 complex can induce antibody in rabbits.

15. However, the art indicates that like an HIV vaccine, none of the currently available HIV immunotherapy is effective for its intended purpose due to the well-known obstacles associated with HIV infection. "The inability to solve fundamental scientific questions is the root cause for why a successful vaccine is not currently within our grasp" (Desrosiers RC. Nature Medicine Vol. 10 (2004; cited in the previous Office action), pp. 221-223, cited in the previous Office action). Some of those obstacles are outlined here:

1) the extensive genomic diversity associated with the HIV retrovirus, due in large part to error prone reverse transcription of its single-stranded RNA genome;

2) the existence of latent forms of the virus;

3) the ability of the virus to "immune escape" from natural and adoptive immunity against the virus,

4) the ability of the virus to develop resistance to antibody-mediated neutralization;

5) the modes of viral transmission, including both cell-to-cell and free virus transmission,

6) the complexity and variation of the elaboration of the disease and,

7) the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences, etc.

16. To date, several clinical trials have been conducted, but in every situation, the immunogen failed to induce protective immunity, failed to control viremia, and failed to protect individuals at a high risk from infection. Moreover, no experimental vaccine candidates so far have been proven to be effective to protect monkeys from SIV infection in animal models.

17. The existence of these obstacles also prevents one of ordinary skill in the art from accepting any vaccine regimen on its face. In order to provide proof of utility with regard to drugs and their uses, either clinical or *in vivo* or *in vitro* data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established. See in re Irons, 340 F. 2d 924,144 USPQ 351 (CCPA 1965), Ex parte Krepelka, 231 USPQ 746 (PTO Bd. Pat. App & Inter.1986) and Ex pane Chwang, 231 USPQ 751 (PTO Bd. Pat. App & Inter. 1986). In the instant case, the *in vitro* data presented in the specification is insufficient to convince one of ordinary skill in the art that the claimed immunogenic complex can be effective for its intended use, which is the production of protective immunity in human to the

prevention or treatment of HIV infection. Thus, one of ordinary skill in the art is not able to use the claimed invention. The rejection is maintained.

Double Patenting

18. (**Prior rejection-maintained**) The rejection of Claims 1-7, 15 and 21 on the ground of nonstatutory obviousness-type double patenting over Claim 1 of US 5,843,454, and Claim 1 of US 5,518,723 **is maintained** for the reasons of record.

19. Applicant acknowledges the rejection and does not wish to prematurely respond.

Remarks

20. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Bo Peng/
Patent Examiner